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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/796,658	03/08/2004	Elizabeth T. Keating	P51095C1	3148

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EXAMINER	
HENLEY III, RAYMOND J	

ART UNIT	PAPER NUMBER
1614	

DATE MAILED: 04/27/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/796,658	KEATING ET AL.	
	Examiner	Art Unit	
	Raymond J. Henley III	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 2* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 2* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *3/8/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

CLAIMS 1-2 ARE PRESENTED FOR EXAMINATION

Applicants' Preliminary Amendment and Information Disclosure Statement filed March 8, 2004 have been received and entered into the application. Accordingly, the specification at page 1 has been amended and the abstract has been entered. Also, as reflected by the attached, completed copy of form PTO-1449, the cited references have been considered.

Specification

The disclosure is objected to because of the following informality:

In the above referenced amendment to the specification, ---, now abandoned--- should be inserted after "7 August 2002".

Appropriate correction is required.

Claim Rejection - 35 USC § 112, Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-2 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

"The primary purpose of this requirement of definiteness of claim language is to ensure that the scope of the claims is clear so the public is informed of the boundaries of what constitutes infringement of the patent. A secondary purpose is to provide a clear measure of what applicants regard as the invention so that it can be determined whether the claimed invention

meets all the criteria for patentability and whether the specification meets the criteria of 35 U.S.C. 112, first paragraph with respect to the claimed invention." (MPEP 2173).

The expression "close in time or remote in time" in claim 1 contains the relative terms "close" and "remote" which render the claim indefinite. In particular, "close" and "remote" are not defined by the claim, the specification does not provide a reasonably clear, deliberate or precise standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. The period of time which is intended to be represented by "close" and/or "remote" has not been identified and to determine whether or not a given period of time between administration of the claimed actives is intended by Applicants to be included in or excluded by the claims would be open to subjective interpretation. Such is inconsistent with the tenor and express requirements of 35 U.S.C. §112, second paragraph and therefore, the claims are deemed properly rejected.

The present specification at page 2, lines 24-25 is noted where it is disclosed that "such is where one drug is administered in the morning and the second drug is administered in the evening". Such disclosure, however, does not render the claims definite. Words and phrases in the claims must be given their "plain meaning" as understood by one having ordinary skill in the art unless defined by Applicant in the specification with "reasonable clarity, deliberateness and precision". (MPEP 2111.01). Here, Applicants' "definition" of the claim terminology is not reasonably clear, deliberate or precise because it employs the expression "such as..." and thus does not specify what other instances of administration may be considered as being sequential.

Claim Rejection - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claim 1 is rejected under 35 U.S.C. 102(e) as being anticipated by Nichtberger (U.S. Patent No. 6,136,804, cited by the Examiner) who teaches a method for the treatment of inflammation which comprises the administration of a composition which comprises a combination of a cyclooxygenase-2 "COX-2" inhibitor, i.e., a sub-class of non-steroidal anti-inflammatory drugs (NSAID), (col. 3, lines 41-52, col. 4, lines 50-54 and 56-58) and an antiplatelet agent, of which dipyridamole is highlighted (col. 17, line 58).

The patentee further teaches an administration schedule believed to be encompassed by the requirement in claim 1 that "the sequential administration is close in time or remote in time" because the patentee teaches that "[t]he instant pharmaceutical combinations comprising an antiplatelet agent in combination with a COX-2 inhibitor includes administration of a single pharmaceutical dosage formulation...as well as administration of each active agent in its own separate pharmaceutical dosage formulation...[which] can be administered at essentially the same time, i.e., concurrently, or at separately staggered times, i.e., sequentially." (col. 23, lines 24-33).

Nichtberger fails to expressly disclose "a PDE4 inhibitor". However, Barnette et al. (U.S. Patent No. 5,998,428, cited by the Examiner) shows in Table I, col. 5, line 30 and describes at col. 6, line 18 that dipyridamole is a PDE 4 inhibitor. Barnette et al. is a secondary reference

properly relied upon to show that a claim element is inherent to dipyridamole. See MPEP § 2131.01.

Claim Rejection - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1 and 2 are rejected under 35 U.S.C. 103(a) as being unpatentable over Barnette et al. (U.S. Patent No. 5,998,428) in view of Collins et al. (U.S. Patent No. 6,096,728), both cited by the Examiner.

Barnette et al. teach a method for treating inflammation in which an inhibitor of PDE IV, i.e., phosphodiesterase type IV, is administered (col. 3, lines 33-41 and 58-67). At col. 5, lines 51-64, the patentees further teach that PDE IV inhibitors having an IC_{50} of about 0.1 or greater are preferentially useful in for treating inflammatory disorders and the PDE IV inhibitor

specified in present claim 2 is identified by the patentees in Table 1, col. 5, 10th cited compound as having an IC_{50} of 1.1, i.e., greater than 0.1.

The difference between the above and the claimed subject matter lies in that the patentees fail to teach the additional administration of a NSAID in general, as required by present claim 1, or the specific NSAIDs of present claim 2.

However, the difference between the subject matter sought to be patented and the prior art is such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains because one of such skill, interested in solving the problem of treating inflammatory disorders, would have been aware of not only the Barnette et al. reference, but Collins et al. (U.S. Patent No. 6,096,728) as well. One of ordinary skill in the art having before them Barnette et al. and Collins et al. would have been motivated to combine a PDE IV inhibitor and an NSAID in the manner presently claimed in order to treat an inflammatory disorder.

In particular, Collins et al. teach the additional administration of the NSAIDs of present claim 2 with an active agent having a different mechanism of action in order to treat inflammatory disorders which would have motivated one of ordinary skill in the art to modify the method of Barnette et al. to include the administration of a NSAID so as to obtain at least similar results achieved by Collins et al. See Collins et al. at col. 28, lines 20-52 where it is taught that NSAIDs may be combined with an interleukin, i.e., IL, -1 inhibitor. In Barnette et al., the active agent, i.e., a PDE IV inhibitor, also has a different mechanism of action from NSAIDs because PDE IV inhibitors inhibit the activity of phosphodiesterase type IV. Also, see Collins et al. at col. 28, line 53 – col. 31, line 12 where the various NSAIDs are listed.

Also supporting the Examiner's conclusion that the claimed subject matter would have been obvious is the fact that each of the claimed actives were known to be useful for treating inflammatory disorders while it has been held that it is considered prima facie obvious to have combined two or more ingredients each of which was known to be useful for the same purpose in order to form a third composition that is useful for the very same purpose. The idea for combining them flows logically from their have been used separately. See In re Kerkhoven 205 U.S.P.Q. 1069 (CCPA 1980) and the cases cited therein. The skilled artisan would have been motivated to combine such ingredients in order to achieve at least additive results and to provide the individual being treated with the most convenient, effective therapy possible.

Accordingly, for the above reasons, the claims are deemed to be properly rejected and none are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Raymond J. Henley III whose telephone number is 571-272-0575. The examiner can normally be reached on M-F, 8:30 am to 4:00 pm Eastern Time.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on 571-272-0951. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR

system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Raymond J Henley III
Primary Examiner
Art Unit 1614

April 24, 2005